REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing claim amendments and following remarks.

Claims 1–34, 58-59, 73, 79–80 and 82–90 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 6,183,780 to Van Balken et al. (Van Balken) in view of U.S. Patent No. 6,120,803 to Wong et al. (Wong). Applicant traverses the rejection of these claims under Section 103(a) over Van Balken in view of Wong and requests that the rejection be withdrawn.

A. Even if Properly Combined, the Combination of Van Balken and Wong does not Result in Applicant's Claimed Tablets

Applicant asserts that there is no motivation or suggestion to combine Van Balken and Wong, and furthermore that the references are not properly combined. This is discussed in more detail below. However, even if there were some motivation or suggestion in Van Balken or Wong to combine their teachings, and assuming, solely for the purposes of argument, that the references were properly combined, such a combination does not provide the presently claimed tablets.

A combination of Van Balken and Wong, as suggested by the Office action, would yield one of the following three possible dosage forms: (a) Van Balken's non-swelling core surrounded by Wong's band; (b) Wong's swellable core surrounded by Van Balken's coating and Wong's band over or under the coating; or (c) dosage form 'b' surrounded by a gastric-emptying delaying agent. None of the proposed dosage forms is applicant's presently claimed tablet.

First, applicant's claim 1 requires that the core be a swellable core that includes an "expandable material or materials." Van Balken's non-swelling core material is clearly distinguishable from applicant's claimed "swellable core" composition having an expandable material or materials. For example, Van Balken describes a core "having no substantial swelling properties upon exposure to gastrointestinal fluids." Column 2, lines 29, 30 (emphasis added). With reference to numbered point 6 of the attached declaration by Linna R. Chen, Ph.D., an expert in the field of pharmaceutical formulations, this requisite feature of Van Balken's technology is reiterated throughout Van Balken's disclosure. For example, Van Balken states that "[t]he overall composition is chosen in such a way that an immediate release carrier, having no substantial swelling properties is obtained." Column 3, lines 39–42 (emphasis added). Thus, dosage form "a" proposed above, having Van Balken's non-

swelling core composition and coating combined with Wong's band, is not the tablet claimed by applicant.

Second, applicant's claim 1 requires that the "outer rupturable coating surrounding the core" comprises a "water-soluble modifier." As explained in numbered paragraph three of the attached Declaration by Professor Ayres, Van Balken's coating does not include a "water-soluble modifier" as featured in applicant's claims. Specifically, Van Balken states at column 4, lines 60–62, that "to prevent release of active substance from the formulation by means of diffusion o[r] permeation, the coating should not comprise substantial amounts of polymeric coating materials that are soluble and/or erodable." Van Balken, column 4, lines 60–62 (emphasis added). Thus, Van Balken's coating does not include water-soluble polymeric materials. As a result, proposed dosage forms 'b' and 'c' above are not the sustained release tablet recited in applicant's claim 1.

Because no combination of features from Van Balken and Wong provides applicant's claimed tablet, the obviousness rejection of claim 1 over Van Balken in view of Wong is improper and should be withdrawn.

Furthermore, a belly band that is made from the same material as the core material, as recited by applicant in claim 1, is not the circumscribing band taught by Wong, which is made from materials other than those used to form Wong's core. Wong's examples feature dosage forms having a band of insoluble material that prevents the banded portion of the dosage form core from swelling. Wong's band is made from "rigid" or "semi-rigid" insoluble polymeric material, such as polyethylene, whereas Wong's core is formed from swellable materials such as hydroxypropylcellulose. The insoluble material used to make Wong's circumscribing band is distinct from both the core and any coating materials disclosed by Wong. In contrast the tablet according to claim 1 features a belly band that s defined by the core. Thus, even though the circumscribing band described by Wong could be used in combination with applicant's claimed dosage form, such circumscribing band is not the belly band referred to in applicant's claim 1. Thus, even if Wong and Van Balken could be properly combined, as alleged by the Office action, to produce a "banded tablet," such a tablet would not have applicant's composition, as defined by applicant's claim 1. Therefore, applicant respectfully requests that the rejection over Van Balken and Wong be withdrawn.

For the reasons stated above, the cited references do not provide the embodiment of applicant's tablet recited in claim 1, or even all o f the components of applicant's claimed tablets. Therefore, even

by picking and choosing various features of the cited references with the benefit of hindsight, one could not prepare the presently claimed tablets.

The Office action alleges that Van Balken teaches the release profile defined in claim 15. Claim 15 has been amended to feature a release profile that does not encompass Van Balken's immediate release profile. For example, claim 15, as amended, recites that from 5 to 40% of the total active ingredient is released after four hours and that from 10 to 80% is released after eight hours. In contrast, Van Balken's immediate release profiles require complete release within a short time period. With reference to the cited Figure, Van Balken's Figure 5, the illustrated release profile indicates 0% drug release at 7 hours (claim 15 requires that at least 5% drug release have occurred by this time) and 100% drug release after about 8 hours (whereas claim 15 states that no more than 80% of drug release occur by this time). Thus, neither the percentage of drug release at 7 hours nor the percentage of drug release after 8 hours comply with applicant's claim features. Similarly, Van Balken's cited Figures 6 and 7 depict drug release profiles outside the parameters recited in claim 15, as amended.

For the reasons stated above, Van Balken and Wong do not teach the features of applicant's claims. Therefore, applicant respectfully requests that the rejection over Van Balken in view of Wong under 35 U.S.C. § 103(a) be withdrawn.

B. The Office action does not Establish a Prima Facie Case of Obviousness

A *prima facie* case of obviousness based upon a combination of references must include some basis for combining the references in the manner alleged to render the claimed invention obvious. No such basis exists for combining Van Balken and Wong.

The Office action appears to rely upon Van Balken's text at column 5, lines 8–13, for the requisite motivation. With reference to the attached Declarations by Linna R. Chen, Ph.D., and Professor Ayres, both of whom are experts in the field of pharmaceutical formulations, the Office action misconstrues the meaning of the cited text. The Office action cites Van Balken as teaching that "the sustained release of a drug is desirable after a pre-determined lag-time." However, Van Balken actually teaches that sustained release is to be avoided. For example, at column 5, lines 4–7, EP 0 655 240 is distinguished from the Van Balken technology because the '240 application describes a coating that is "eroded, leading to an increasing permeability and consequently diffusion of the active substance through the coating." In contrast, according to column 4, lines 60–64, Van Balken's coating

does not comprise substantial amounts of soluble and/or erodable polymeric coating materials for the purpose of preventing "release of active substance from the formulation by means of diffusion o[r] permeation." Therefore, the passage relied upon by the Office action to provide the motivation for combining Van Balken and Wong cannot provide such motivation if read correctly.

The Office action cites no other explicit recitation or implicit teaching of Van Balken or Wong to support their combination. Because Van Balken and Wong do not provide any motivation for their combination, the Office action does not establish a *prima facie* case of obviousness. Applicant therefore respectfully requests that the § 103(a) rejection be withdrawn.

C. The Combination of Wong and Van Balken Destroys their Intended Functions and Therefore the Combination is Improper

Combining Van Balken and Wong's teachings as suggested by the Office action would destroy the intended function underlying each of Van Balken's and Wong's dosage forms, and thus the references are not combinable. "A proposed modification [is] inappropriate for an obviousness inquiry when the modification render[s] the prior art reference inoperable for its intended purpose." *In re Fritch*, 972 F.2d 1260, 1265 n.12 (Fed. Cir. 1992), 23 U.S.P.Q.2d 1780, 1783 n.12. Van Balken's intended function is "Delayed Immediate Release" as is stated in the title, abstract and throughout the specification. Thus, Van Balken is directed to a dosage form that provides rapid, complete release following a preselected lag time of known, predictable duration. See, e.g., Van Balken's Figure 1, where zero drug release is shown until hour 10 and 100% drug release is shown at hour 11.

Contrarily, Wong is directed to a dosage form that is retained in the stomach, and reportedly exhibits sustained release without a lag time. See, e.g., Wong's Figure 8, where drug release begins immediately (at time zero) and continues for several hours. Thus, the dosage forms of Van Balken and Wong are formulated to provide mutually exclusive release rates, and there is no suggestion that combining elements of the two different dosage forms would be desirable or would be successful.

For example, if Wong's core composition were coated with Van Balken's coating composition, Wong's core composition would not contact gastric fluid and hence would not hydrate or swell sufficiently to be retained in the stomach. Thus, because the dosage form produced by combining the two references would not swell, the combination would destroy Wong's intended function of gastric retention, and therefore the references are not properly combinable. The Office action asserts that

Wong provides methods for gastric retention that do not require swelling. Specifically, the Office action states that "a polymer matrix tube or ring may be provided, the ends of which would flare outwardly, resulting in a larger effective diameter of the dosage form." However, with reference to the attached Declaration by Professor Ayres, an expert in the field of pharmaceutical formulations, this method still requires polymer swelling. See Wong at column 7, line 54 "swellable polymer matrix" (emphasis added) and column 7, lines 62–64,"the ends of the polymer tube or ring flaring outwardly and swelling to provide a larger effective diameter" (emphasis added). Thus, the Office action has misinterpreted the cited section of Wong as teaching a swelling-independent mechanism for gastric retention. The dosage form must swell to be retained in the stomach, and must contact gastric fluid to swell. Thus, Van Balken's coating would render Wong's dosage forms inoperable for gastric retention and therefore the references are not properly combinable.

The Office action also argues that a gastric-emptying delaying agent could be used to facilitate gastric retention, thus providing a swelling-independent method for ensuring gastric retention. However, Wong does not teach that a gastric-emptying delaying agent can used alone to ensure gastric retention. Rather, with reference to numbered points seven and nine, respectively, of the attached Declarations by Linna R. Chen, Ph.D. and by Professor Ayres, Wong appears to teach that a gastric-emptying delaying agent is merely a supplementary method to swelling.

Moreover, if a swellable polymer matrix as taught by Wong were used as a tablet core and the core was coated with Van Balken's coating composition, the resulting tablet likely would exhibit, as discussed by Van Balken at column 1, lines 55–61, unpredictable lag times and would not yield pulsatile release. This combination of features would be directly contrary to the result Van Balken's dosage form is designed to achieve.

Furthermore, Van Balken distinguishes formulations having swellable core materials, and teaches that swellable core materials are inoperative for use with his disclosed coating for achieving delayed immediate release. Please see numbered point four of the attached Rule 132 Declaration by Linna R. Chen, Ph.D. Dr. Chen avers that Van Balken's coating in combination with a swellable core composition would not provide sustained release following a predetermined lag time. Van Balken teaches that swellable core materials are unsuitable for providing delayed immediate release. Thus, a combination comprising Wong's core and Van Balken's coating would destroy Van Balken's intended function of delayed immediate (pulsatile) release, as well as Wong's intended function of gastric

retention, and hence the references are not properly combinable. Therefore, applicant respectfully requests that the rejection over Van Balken in view Wong be withdrawn.

If a core composition having no substantial swelling properties as taught by Van Balken were surrounded by a band of insoluble material as taught by Wong, the core would rapidly disintegrate upon contact with gastrointestinal fluid and not provide any delayed release or gastric retention of the tablet. Thus, the combination would destroy both Van Balken's and Wong's intended functions, and the references are not properly combinable.

Claims 30–34 depend from claim 3, which recites an over coating of an active ingredient. Neither Van Balken nor Wong teaches an over coating comprising an active ingredient. The combination of Van Balken and Wong therefore cannot teach the embodiment recited in claim 3. Indeed, such an over coating would be inconsistent with Van Balken's stated goal of "Delayed Immediate Release." For example, placing an active ingredient in Van Balken's coating material likely would result in immediate release of the active ingredient without any lag time. Alternatively, such a coating conceivably could result in sustained release without a lag time. Both results are inconsistent with Van Balken's stated goal of "delayed immediate release." Thus applicant maintains that claims 30–34 are patentable for these reasons and further in view of the patentable combinations of features recited in these claims.

D. Conclusion

In summary, even if Van Balken and Wong were combinable, the combination would not provide applicant's claimed tablets. Moreover, Van Balken should not be combined with Wong as alleged by the Office action for at least two reasons. One, no motivation or suggestion is provided sufficient to justify the combination. And two, if, for purposes of argument, the teachings of Van Balken and Wong were combined, the combination would undermine the stated objectives of both Van Balken and Wong. Therefore, the rejection under 35 U.S.C. § 103(a) over Van Balken in view of Wong is improper, or, in the alternative, has been overcome, and therefore applicant respectfully requests that the rejection be withdrawn.

Respectfully submitted,

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